REMARKS

Claims 30, 31, 36 and 37 are pending and stand rejected. The Examiner has made a number of rejections. We list them here in the order in which they are addressed:

(1) Claims 30, 31, 36 and 37 are rejected under the judicially created doctrine of double patenting over claims 1-9 of U.S. Patent No. 5,874,087.

(2) Claims 30, 31, 36 and 37 are rejected under the judicially created doctrine of double patenting over claims 22-28 of U.S. Patent No. 5,958,422.

(3) Claims 30, 31, 36 and 37 are rejected under the judicially created doctrine of double patenting over claims 20-23 of U.S. Patent No. 5,596,132.

(4) Claims 30, 31, 36 and 37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(5) Claims 30, 31, 36 and 37 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent 5,316,931.

(6) Claims 30, 31, 36 and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Chapman, *et al.*, *The Plant Journal*, 2:549-557, 1992.

Applicant believes that the following remarks traverse the Examiner's rejection of the claims. These remarks are presented in the same order as they appear above.

I. CLAIMS 30, 31, 36 and 37 ARE NOT SUBJECT TO A DOUBLE PATENTING REJECTION

A. The Claims are Patentably Distinct from U.S. 5,874,087

The Examiner rejected Claims 30, 31, 36 and 37 under the judicially created doctrine of double patenting over claims 1-9 of U.S. Patent 5,874,087 stating that the claims are not

patentably distinct over the claims of the prior art reference. The Applicants respectfully disagree.

> A double patenting rejection of the obvious-type (*i.e.*, non-statutory) is "analogous to [a failure to meet] the nonobviousness requirement of 35 U.S.C. 103" except that the patent principally underlying the double patenting rejection is not considered prior art. *MPEP* 804(II)(B)(1).

In this regard, the Claims of the instant specification are directed to a nonobviousness, improved method wherein the insertion of the sequence encoding the foreign peptide is made in such a way as to ensure that it is "free from direct sequence repeats flanking said insert" thereby avoiding genetic instability (see, for example, pages 3 and 9). The '087 patent has no such claim language. Based on this difference between the Claims in the prior art patent and the Claims in the present application, the Examiner's rejection must fail.

B. The Claims are Patentably Distinct from U.S. 5,958,422

The Examiner rejected Claims 30, 31, 36 and 37 under the judicially created doctrine of double patenting over claims 22-28 of U.S. Patent 5,958,422 stating that the claims are not patentably distinct over the claims of the '422. The Applicants respectfully disagree. The '422 Claims are species claims. This is in contrast to the present application wherein the claims are drawn to a genus. Claim 30 of the present application is drawn to the modification of "plant virus particles". In the specification, examples are drawn to these eight different viruses in 7 different genuses: cowpea mosaic virus (CPMV, genus *comovirus*), sesbania mosaic virus (SBMV, genus *sobemovirus*), lucerne transient streak virus (LTSV, genus *sobemovirus*), red clover necrotic mosaic virus (RCNMV, genus *dianthovirus*), tobacco mosaic virus (TMV, genus *tobamovirus*), Potato virus X (PVX, genus *potexvirus*), plum pox virus (PPV, genus *potyvirus*) and tobacco rattle virus (TRV, genus *tobravirus*) which are members of a diverse group of viruses including *comoviruses, sobemoviruses, polyomaviridae.* Case law is clear that a prior issuing species claim is not grounds for the rejection based on obviousness-type double patenting. In *Ex parte Harold* [44 USPQ 84, 85 (Pat. Off. Bd. App. 1938)] it was held:

> The fact that claims to a species have been granted in a patent is no bar to the grant of generic claims in a subsequent patent, provided other species are disclosed therein.

More recently, in *Ex parte Michno* [38 USPQ 2d 1211, 1212 (B.P.A.I. 1993)] it was concluded:

> We are unaware of any judicial precedent which stands for the proposition that an obviousness-type double patenting situation automatically arises when a patent on a narrow invention issues during pendency of an application for a claimed invention which encompasses or dominates the narrow invention. The notion that a pending claim to a generic invention is necessarily patentably indistinct, in the sense of double patenting of the obviousness type, from a narrower patented claim encompassed by the pending generic claim was **scotched** by *In re Braat*, 937 F.2d 589 at 594, 19 USPQ2d 1289 at 1293 (Fed. Cir. 1991). (emphasis added).

In light of this consistent precedence, the Examiners rejection of Claims 30, 31, 36 and 37 in the present application must fail.

C. The Claims are Patentably Distinct from U.S. 5,596,132

The Examiner rejected Claims 30, 31, 36 and 37 under the judicially created doctrine of double patenting over claims 1-9 of U.S. Patent 5,874,087 stating that the claims are not patentability distinct over the claims of the '132 patent. The Applicants respectfully disagree.

> A double patenting rejection of the obvious-type (*i.e.*, non-statutory) is "analogous to [a failure to meet] the nonobviousness requirement of 35 U.S.C. 103" except that the patent principally underlying the double patenting rejection is not considered prior art. *MPEP* 804(II)(B)(1).

In this regard, the Claims of the instant specification are directed to a nonobviousness, improved method wherein the insertion of the sequence encoding the foreign peptide is made in such a way as to ensure that it is "free from direct sequence repeats flanking said insert" thereby avoiding genetic instability (see, for example, pages 3 and 9). The '132 patent has no such claim language. Based on this difference between the '132 Claims the Claims in the present application, the Examiner's rejection must fail.

II. CLAIMS 30, 31, 36 and 37 ARE PATENTABLE UNDER 35 U.S.C. 112

The Examiner rejected Claims 30, 31, 36 and 37 as being indefinite. Claims 31, 36 and 37 are dependent on independent Claim 30. The Examiner states that there is insufficient antecedent basis for various limitations in the claim. The Applicants respectfully disagree. However, in order to further the business interests of the applicant and while reserving the

right to prosecute the original or similar claims in the future, Claim 30 has been rewritten. The Claims are now definite and should pass to allowance.

III. THE CLAIMS ARE NOT ANTICIPATED

A. The Claims are not Anticipated by U.S. Patent 5,316,931

The Examiner has rejected Claims 30, 31, 36 and 37 under 35 U.S.C. 102(e) as anticipated by U.S. Patent 5,316,931. The Applicants respectfully disagree. The MPEP states that "to anticipate a claim, the reference must teach every element of the claim". MPEP § 2131. The present application claims the production of modified plant viruses by a method that is an improvement over the cited reference. For example, the present invention claims and the specification teaches a technique that ensures that the site of insertion of the sequence encoding the foreign peptide is "free from direct sequence repeats flanking said insert" thereby avoiding genetic instability (see, for example, pages 3 and 9). This teching is missing from the cited reference. Thus, the reference cited by the examiner does not teach every element as claimed in the present invention, as required, and, therefore, the Examiner's rejection of Claims 30, 31, 36 and 37 must fail.

B. The Claims are not Anticipated by Chapman, *et al*

The Examiner has rejected Claims 30, 31, 36 and 37 under 35 U.S.C. 102(b) as anticipated by Chapman, *et al.*. The Applicants respectfully disagree. The MPEP states that "to anticipate a claim, the reference must teach every element of the claim". §MPEP 2131. The Examiner is invited to carefully compare the Chapman reference with the instant specification. The present application claims the production of modified plant viruses by a method that is a significant improvement over the method in the cited reference. For example, the present invention claims and the specification teaches a technique that ensures that the site of insertion of the sequence encoding the foreign peptide is "free from direct sequence repeats flanking said insert" thereby avoiding genetic instability (see, for example, pages 3 and 9). This element is missing from the cited reference. Thus, the reference cited by the examiner does not anticipate every element as claimed in the present invention, as required, and, therefore, the Examiner's rejection of Claims 30, 31, 36 and 37 must fail.

CONCLUSION

The Applicant believes that the arguments and claim amendments set forth above traverse the Examiner's rejections and, therefore, request that these grounds for rejection be withdrawn for the reasons set above. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, the Applicants' encourage the Examiner to call the undersigned collect at 617.252.3353.

Dated: December 31, 2001

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APPENDIX I
MARKED-UP VERSION OF AMENDED CLAIMS
PURSUANT TO 37 CFR § 1.121 (c)(1)(ii)

The Following is a version of the claims pursuant to 37 C.F.R. § 1.121(c)(1)(ii) with markings showing the changes made herein to the previous version of record of the claims.

30. A method for producing plant virus particles comprising: a) providing i) plant viral nucleic acid comprising nucleic acid which codes for [the] a coat protein, ii) a foreign nucleotide sequence coding for a foreign peptide; b) modifying said plant viral nucleic acid by inserting said foreign nucleotide sequence coding for a foreign peptide at a site within said plant viral nucleic acid which codes for the coat protein so as to create modified viral nucleic acid comprising an insert, wherein said site [of said insert] is free from direct sequence repeats flanking said insert; c) infecting plant material selected from the group consisting of plants, plant tissue, plant cells and protoplasts with said modified viral nucleic acid to produce assembled particles of a modified virus; and d) harvesting assembled particles of the modified virus from said plant material.

APPENDIX II

CLEAN VERSION OF THE ENTIRE SET OF PENDING CLAIMS PURSUANT TO 37 CFR § 1.121 (c)(3)

The Following is a version of the claims pursuant to 37 C.F.R. § 1.121(c)(3) showing a clean version of the pending claims.

30. A method for producing plant virus particles comprising: a) providing i) plant viral nucleic acid comprising nucleic acid which codes for a coat protein, ii) a foreign nucleotide sequence coding for a foreign peptide; b) modifying said plant viral nucleic acid by inserting said foreign nucleotide sequence coding for a foreign peptide at a site within said plant viral nucleic acid which codes for the coat protein so as to create modified viral nucleic acid comprising an insert, wherein said site is free from direct sequence repeats flanking said insert; c) infecting plant material selected from the group consisting of plants, plant tissue, plant cells and protoplasts with said modified viral nucleic acid to produce assembled particles of a modified virus; and d) harvesting assembled particles of the modified virus from said plant material.

31. The method according to claim 30, in which the insert is an addition to said coat protein.

36. The method according to claim 30, in which the foreign nucleotide sequence is inserted by i) selecting two different restriction enzyme sites in the plant viral nucleic acid; ii) cutting the plant viral nucleic acid using the corresponding restriction enzymes; and iii) inserting into the cut viral nucleic acid a pair of complementary oligonucleotides which encode the foreign peptide and which terminate in ends compatible with the restriction enzyme cutting sites.

37. A method according to claim 36, in which in the complementary oligonucleotides, the sequence encoding the foreign peptide is flanked by plant virus-specific sequences so that the foreign nucleotide sequence is inserted as an addition to the plant viral nucleic acid.

Appendix III

MARKED-UP VERSION OF REWRITTEN PARAGRAPHS

PURSUANT TO 37 C.F.R. § 1.121(b)(1)(iii)

On page 1:

In accordance with the provisions of 35 U.S.C. 120, this application claims the priority and is a continuation-in-part of U.S. Patent Application Nos. 08/471,048, filed June 6th, 1995; 08/612,858, filed June 5th, 1996; 08/137,032, filed December 15th, 1993, which is a 371 of PCT/GB20/00589, filed April 2nd, 1992, which claims benefit of the priority under 35 U.S.C. 119 of: Great Britain Patent Application No. 91 08386.5, filed April 16, 1991.

On page 15:

Figure 2a and 2b depicts (A) the sequence of the oligonucleotide used in the construction of pFMDV together with the amino acid sequence encoded by the top (positive) strand, which corresponds to amino acid residues 136-160 from VP1 of FMDV serotype O_1, and (B) the structure of VP23 after insertion of the FMDV-specific oligonucleotides. The arrowed region indicates the extent of the inserted FMDV epitope. The *Nhe*1 site not restored during the cloning is indicated by x*Nhe*1. The diagnostic *Bgl* II site present in the inserted sequence is also indicated.

On page 16:

Figure 5a and 5b depicts (A) the nucleotide sequence if the oligonucleotides used in the construction of pMT7-HIV together with the amino acid sequence encoded by the top (positive) strand which corresponds to amino acid residues 735-752 from gp41 of HIV1, and (B) the sequence of VP23 after insertion of the HIV-specific oligonucleotides. The arrowed region indicates the extent of the inserted HIV epitope. The *Pvu* 1 site present in the inserted sequence is also indicated.

Figure 6a and 6b depicts (A) the nucleotide sequence if the oligonucleotides used in the construction of pMT7-HRV together with the amino acid sequence encoded by the top (positive) strand which corresponds to amino acid residues 85-99 from VP1 of HRV-14, and (B) the sequence of VP23 after insertion of the HRV-specific oligonucleotides. The arrowed region indicates the extent of the inserted HRV epitope. The *Cla* 1 site present in the inserted sequence is also indicated.

On page 17:

Fig[.]ure 10 is a simple line drawing of the solved β-barrel containing virus structures showing the secondary structural elements which make up the coat protein domains.

Fig[.]ure 11a and 11b shows the (A) nucleotide and (B) protein sequences of SBMV surrounding a potential insertion site.

Fig[.]ure 12 shows a comparison of the βH-βI loop of three sobemoviruses. Conserved residues are highlighted in bold and the locations of the loops and β-strands are indicated.

Fig[.]ure 13a and 13b shows the (A) nucleotide and (B) protein sequences of LTSV surrounding a potential insertion site.

Fig[.]ure 14 illustrates alignment of the coat protein sequences of RCNMV and TBSV using a Lopman-Person alignmnent algorithm.

Fig[.]ure 15 illustrates a Chou-Fasman β-region prediction plot of RCNMV residues 214-257 using an algorithm based upon the structures found in 64 proteins.

Fig[.]ure 16 illustrates application of the EMBL PHDsec algorithm program to the same RCNMV sequence as shown in Figure 15.

Fig[.]ure 17a and 17b shows the (A) nucleotide and (B) protein sequences of RCNMV surrounding a potential insertion site.

Fig[.]ure 18a and 18b shows (B) five deletion constructs and (A) an unmodified clone of TRV as described in Example 13.

On page 22:

The construction and properties of plasmids pBT7-123, pMT7-FMDV-I and pMT7-FMDV-II have been described previously (Usha, *et al.*, 1993). These constructs and their derivatives were propagated in *Escherichis coli* strain JM83. Oligonucleotides were synthesized on a Pharmacia [Gene Assembler Plus] GENE ASSEMBLER PLUS™ synthesizer. Sequence analysis was performed by "dideoxy" method using either *E. coli* DNA polymerase I (Klenow fragment) or Sequenase™ version 2.0.